

IN THE CLAIMS:

Amend the claims as follows.

Claims 1-14. (Canceled)

15. (Previously Presented) A modified polypeptide having human granulocyte colony stimulating factor activity (hG-CSF),

(a) wherein at least one group of the carboxyl, mercapto or guanidino group in the molecule of the polypeptide is chemically modified with a polyalkylene glycol derivative; or

(b) wherein the polypeptide has the amino acid sequence of SEQ ID NO:1, wherein at least one group of the amino, carboxyl, mercapto or guanidino group in the molecule of the polypeptide is chemically modified with a polyalkylene glycol derivative.

16. (Previously Presented) The modified polypeptide according to claim 15,

(a) wherein at least one amino acid of the 1st to 6th and 17th amino acids from the N terminus side in the amino acid sequence of SEQ ID NO:1 is replaced by another amino acid; or

(b) wherein at least one of the 1st to 11th amino acids from the N terminus side in the amino acid sequence of SEQ ID NO:1 is deleted and the 17th amino acid thereof is optionally replaced by Ser.

17. (Previously Presented) The modified polypeptide according to claim 15, wherein the amino acid sequence of the polypeptide has, from the N terminus,

(a) Glu in the third position, Lys in the fourth position, Ser in the fifth position and Ser in the seventeenth position,

- (b) Val in the first position, Ile in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (c) Cys in the first position, Ile in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (d) Tyr in the first position, Ile in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (e) Arg in the first position, Thr in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (f) Thr in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (g) Asn in the first position, Glu in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (h) Ile in the first position, Thr in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (i) Ser in the first position, Thr in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (j) Arg in the fourth position and Ser in the seventeenth position,
- (k) Ala in the first position, Thr in the third position, Tyr in the fourth position, Arg in the fifth position and Ser in the seventeenth position, or
- (l) Ser in the seventeenth position.

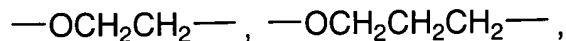
18. (Previously Presented) The modified polypeptide according to claim 15, wherein the amino acid sequence of the polypeptide has Ala in the first position, Thr in the third position, Tyr in the fourth position, Arg in the fifth position and Ser in the seventeenth position from the N terminus.

19. (Previously Presented) The modified polypeptide according to claim 15, wherein the polyalkylene glycol derivative is selected from the consisting of a polyethylene glycol derivative, polypropylene glycol derivative, and a derivative of polyethylene glycol-polypropylene glycol copolymer.

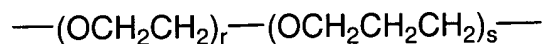
20. (Previously Presented) The modified polypeptide according to claim 15, wherein the amino group is modified with a polyalkylene glycol derivative having the formula (I):



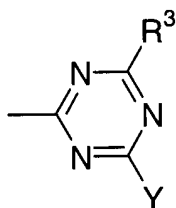
wherein R^1 represents an alkyl or alkanoyl group; M represents the formula:



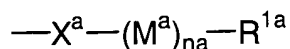
or



wherein r and s have any variable positive integral values, which are the same or different; n has any variable positive integral values; X represents a single bond, O, NH, or S; and R^2 represents the formula:

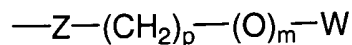


wherein R^3 represents OH, halogen, or the formula:

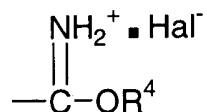


wherein X^a , M^a , R^{1a} and na are identical to said X, M, R^1 and n, respectively, and

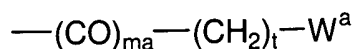
Y represents halogen or the formula:



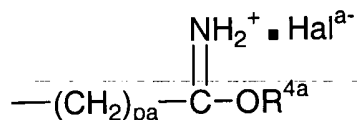
wherein Z represents O, S, or NH; W represents a carboxyl group, an active derivative thereof, or the formula:



wherein R^4 represents an alkyl group; and Hal represents halogen, and p has an integral value of 1 to 6; and m has a value of 0 or 1,



wherein W^a and ma are identical to said W and m, respectively; and t has an integral value of from 0 to 6, or



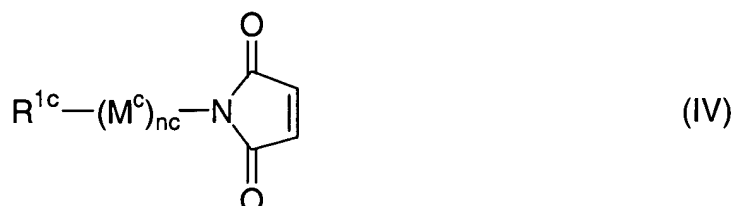
wherein Hal^a , pa and R^{4a} are identical to said Hal, p and R^4 , respectively.

21. (Previously Presented) The modified polypeptide according to claim 15, wherein the carboxyl group is modified with a polyalkylene glycol derivative having the formula (III):



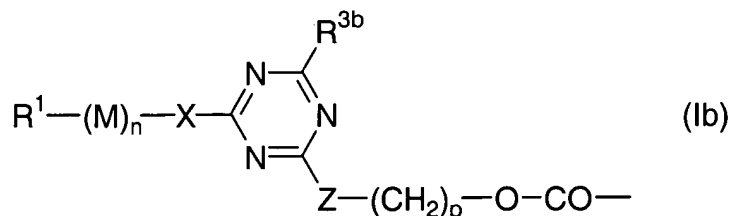
wherein M^b , R^{1b} and nb are identical to said M, R^1 and n, respectively.

22. (Previously Presented) The modified polypeptide according to claim 15, wherein the mercapto group is modified with a polyalkylene glycol derivative having the formula (IV):

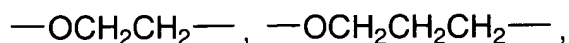


wherein M^c , R^{1c} , and nc are identical to said M , R^1 , and n , respectively.

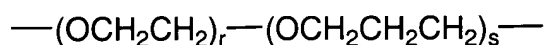
23. (Previously Presented) A modified polypeptide having human granulocyte colony stimulating factor activity (hG-CSF), wherein at least one group amino group in the formula is substituted with a group of the formula (Ib):



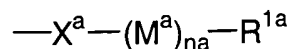
wherein R^1 represents an alkyl or alkanoyl group; M represents the formula:



or



wherein r and s have any variable positive integral values, which are the same or different, n has any variable positive integral value; X represents a single bond, O, NH, or S; R^{3b} represents OH, halogen, or the formula:



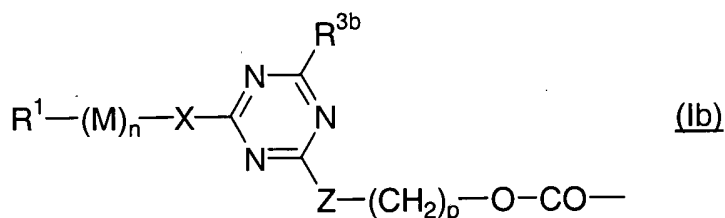
wherein X^a , M^a , R^{1a} and na are identical to said X , M , R^1 and n , respectively; Z represents O, S, or NH; and p has an integral value of from 1 to 6.

24. (Currently Amended) A method for treating a patient with decreased platelet counts comprising administering an effective amount of:

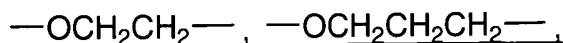
(a) a modified polypeptide having human granulocyte colony stimulating factor activity (hG-CSF), wherein at least one group of the amino, carboxyl, mercapto or guanidino group in the molecule of the polypeptide is chemically modified with a polyalkylene glycol derivative or a styrene-maleic acid copolymer;

(b) a modified polypeptide having human granulocyte colony stimulating factor activity (hG-CSF) having the amino acid sequence of SEQ ID NO:1, wherein at least one group of the amino, carboxyl, mercapto or guanidino group in the molecule of the polypeptide is chemically modified with a polyalkylene glycol derivative or a styrene-maleic acid copolymer; or

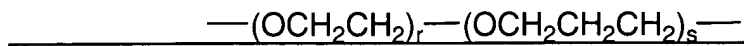
(c) the modified polypeptide of claim 23 having human granulocyte colony stimulating factor activity (hG-CSF), wherein at least one group amino group in the formula is substituted with a group of the formula (Ib):



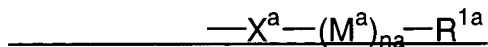
wherein R^1 represents an alkyl or alkanoyl group; M represents the formula:



or



wherein r and s have any variable positive integral values, which are the same or different, n has any variable positive integral value; X represents a single bond, O, NH, or S; R^{3b} represents OH, halogen, or the formula:



wherein X^a, M^a, R^{1a} and na are identical to said X, M, R¹ and n, respectively; Z represents O, S, or NH; and p has an integral value of from 1 to 6.

25. (Previously Presented) The method according to claim 24,

(a) wherein at least one amino acid of the 1st to 6th and 17th amino acids from the N terminus side in the amino acid sequence of SEQ ID NO:1 is replaced by another amino acid; or

(b) wherein at least one of the 1st to 11th amino acids from the N terminus side in the amino acid sequence of SEQ ID NO:1 is deleted and the 17th amino acid thereof is optionally replaced by Ser.

26. (Previously Presented) The method according to claim 24, wherein the amino acid sequence of the polypeptide has, from the N terminus,

(a) Glu in the third position, Lys in the fourth position, Ser in the fifth position and Ser in the seventeenth position,

(b) Val in the first position, Ile in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,

(c) Cys in the first position, Ile in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,

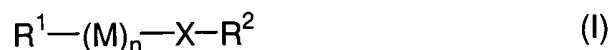
- (d) Tyr in the first position, Ile in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (e) Arg in the first position, Thr in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (f) Thr in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (g) Asn in the first position, Glu in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (h) Ile in the first position, Thr in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (i) Ser in the first position, Thr in the third position, Arg in the fourth position, Ser in the fifth position and Ser in the seventeenth position,
- (j) Arg in the fourth position and Ser in the seventeenth position,
- (k) Ala in the first position, Thr in the third position, Tyr in the fourth position, Arg in the fifth position and Ser in the seventeenth position, or
- (l) Ser in the seventeenth position.

27. (Previously Presented) The method according to claim 24, wherein the amino acid sequence of the polypeptide has Ala in the first position, Thr in the third position, Tyr in the fourth position, Arg in the fifth position and Ser in the seventeenth position from the N terminus.

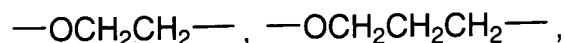
28. (Previously Presented) The method according to claim 24, wherein the polyalkylene glycol derivative is selected from the group consisting of a polyethylene glycol derivative, a polypropylene glycol derivative, and a derivative of polyethylene glycol-polypropylene glycol copolymer.

29. (Previously Presented) The method according to claim 24, wherein the amino group is modified with

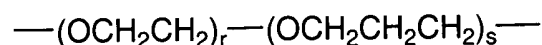
(a) a polyalkylene glycol derivative having the formula (I):



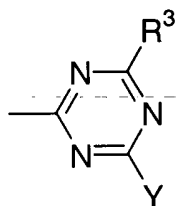
wherein R^1 represents an alkyl or alkanoyl group; M represents the formula:



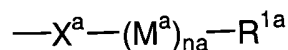
or



wherein r and s have any variable positive integral values, which are the same or different; n has any variable positive integral values; X represents a single bond, O, NH, or S; and R^2 represents the formula:

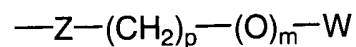


wherein R^3 represents OH, halogen, or the formula:

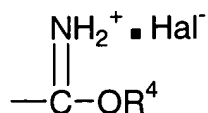


wherein X^a , M^a , R^{1a} and na are identical to said X, M, R^1 and n, respectively, and

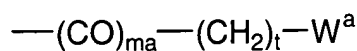
Y represents halogen or the formula:



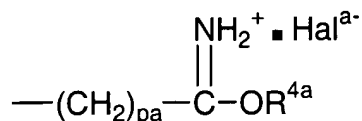
wherein Z represents O, S, or NH; W represents a carboxyl group, an active derivative thereof, or the formula:



wherein R^4 represents an alkyl group; and Hal represents halogen, and p has an integral value of 1 to 6; and m has a value of 0 or 1,

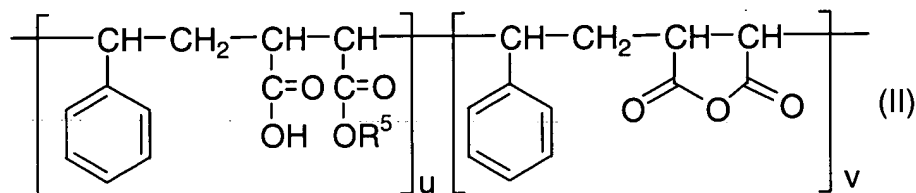


wherein W^a and m^a are identical to said W and m, respectively; and t has an integral value of from 0 to 6, or



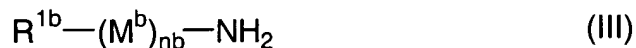
wherein Hal^a , p^a and R^{4a} are identical to said Hal, p and R^4 , respectively, or

(b) a styrene-maleic acid copolymer having the formula (II):



wherein u and v have any variable positive integral values, which are the same or different; and R^5 represents a hydrogen atom, or an alkyl group.

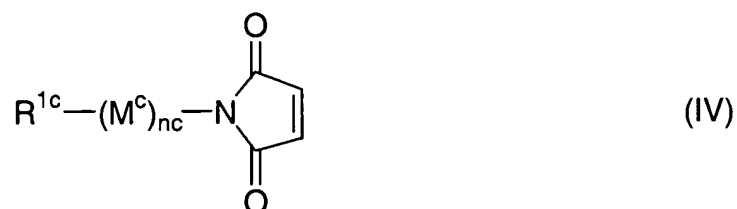
30. (Previously Presented) The method according to claim 24, wherein the carboxyl group is modified with a polyalkylene glycol derivative having the formula (III):



wherein M^b , R^{1b} and nb are identical to said M, R^1 and n, respectively.

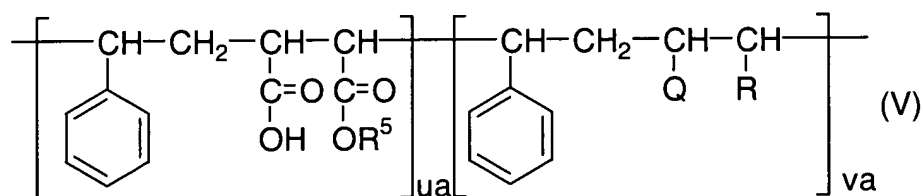
31. (Previously Presented) The method according to claim 24, wherein the mercapto group is modified with

- (a) a polyalkylene glycol derivative having the formula (IV):

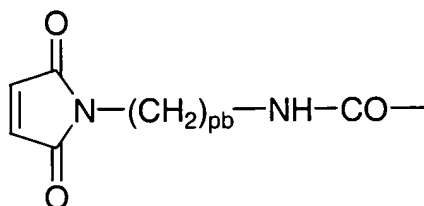


wherein M^c , R^{1c} , and nc are identical to said M , R^1 , and n , respectively, or

- (b) a styrene-maleic acid copolymer having the formula (V):

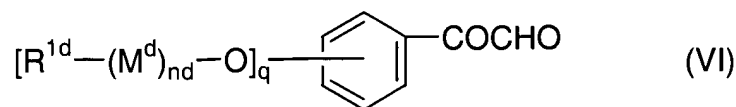


wherein R^{5a} , ua , and va are identical to said R^5 , U , and V , respectively, and one of Q and R represents a carboxyl group, and the other represents the formula:



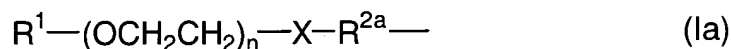
wherein pb is identical to said p .

32. (Previously Presented) The method according to claim 24, wherein the guanidino group is modified with a polyalkylene glycol derivative having the formula (VI):

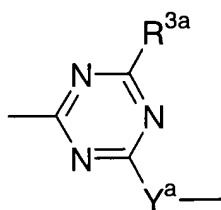


wherein q has a value of 1 or 2, and M^d , R^{1d} , and nd are identical to said M, R^1 , and n, respectively.

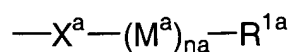
33. (Previously Presented) The method according to claim 24, wherein the amino group is modified by binding to a group represented by the formula (Ia):



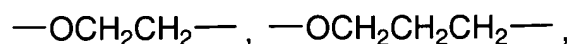
wherein R^1 represents an alkyl or alkanoyl group; n has any variable positive integral value; X represents a single bond, O, NH, or S; R^{2a} represents the formula:



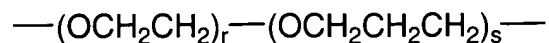
wherein R^{3a} represents OH, halogen, or the formula:



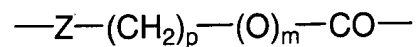
wherein X^a , R^{1a} and na are identical to said X, R^1 and n, respectively, M^a represents the formula:



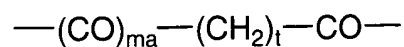
or



wherein r and s have any variable positive integral values, which are the same or different, and Y^a represents a single bond, the formula:



wherein Z represents O, S, or NH; p has an integral value of from 1 to 6; and m has a value of 0 or 1, or the formula:



wherein ma is identical to said m; and t has an integral value of from 0 to 6.